

*DAC*  
*LMW*

PATENT  
ATTORNEY DOCKET NO. 07588/008001

Certificate of Mailing: Date of Deposit: February 2, 2005

I hereby certify under 37 C.F.R. § 1.8(a) that this correspondence is being deposited with the United States Postal Service as **first class mail** with sufficient postage on the date indicated above and is addressed to Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Christine M. Colbert

Printed name of person mailing correspondence

*Christine M. Colbert*

Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Morey Kraus et al.	Art Unit:	1632
Serial No.:	09/698,893	Examiner:	Anne-Marie Falk, Ph.D.
Filed:	October 27, 2000	Customer No.:	21559
Title:	METHODS FOR IMPROVING CENTRAL NERVOUS SYSTEM FUNCTIONING		

Mail Stop Petition  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

PETITION TO WITHDRAW NOTICE OF ABANDONMENT

Under 37 C.F.R. §§ 1.8(b) and 1.181, Applicants hereby petition to have the Notice of Abandonment that was mailed in connection with the above-captioned case on January 25, 2005 withdrawn. A copy of the Notice is enclosed. According to the Notice, the application was abandoned under 37 C.F.R. § 1.135 for Applicants' failure to reply to an Office action that was mailed on July 13, 2004. However, as explained below, a reply was timely filed on January 13, 2005.

The undersigned, Applicants' attorney of record, first became aware of the abandonment on January 25, 2005, upon receipt of the Notice of Abandonment and

submits that this petition to withdraw the Notice is being promptly submitted as required by 37 C.F.R. § 1.8(b)(1).

The following documents are submitted under 37 C.F.R. § 1.8(b)(2) as proof that a reply was timely filed on January 13, 2005:

1. A copy of the reply, including an executed certificate of mailing signed by Tracey Simmons on January 13, 2005.
2. A copy of the Petition for Extension of Time, including an executed certificate of mailing signed by Tracey Simmons on January 13, 2005, which extended the period for replying to the Office Action for three months, to and including January 13, 2005.
3. A copy of a check dated January 13, 2005 and postcard dated January 13, 2005 that were included with the reply and Petition for Extension.
4. A copy of the postcard that was stamped as having been received by the PTO Mailroom on January 18, 2005.

Also enclosed are original signed declarations under 37 C.F.R. § 1.8(b)(3) by:

1. Paul T. Clark, attesting on the basis of personal knowledge that the above documents were timely filed on January 13, 2005.
2. Tracey Simmons, attesting on the basis of personal knowledge that the above documents were timely filed on January 13, 2005.
3. Elvis De La Cruz, attesting on the basis of personal knowledge to the mail procedures in effect on January 13, 2005.

Applicants submit that the reply was timely filed and requests that the Notice of Abandonment be withdrawn.

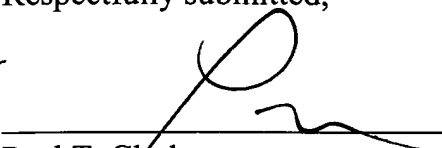
If there are any charges or any credits, please apply them to Deposit Account No.

03-2095.

Respectfully submitted,

Date:

Feb. 2, 2005

  
\_\_\_\_\_  
Paul T. Clark  
Reg. No. 30,162

Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045



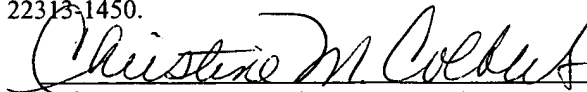
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Christine M. Colbert

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Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Morey Kraus et al.

Art Unit: 1632

Serial No.: 09/698,893

Examiner: Anne-Marie Falk, Ph.D.

Filed: October 27, 2000

Customer No.: 21559

Title: METHODS FOR IMPROVING CENTRAL NERVOUS SYSTEM  
FUNCTIONING

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Commissioner for Patents  
P.O. Box 1450  
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DECLARATION OF PAUL T. CLARK

I, Paul T. Clark, declare as follows:

I am a partner in the law firm of Clark & Elbing LLP and an attorney of record in the above-captioned application.

I first became aware of the abandonment of the above-captioned application on January 25, 2005, upon receipt of a Notice of Abandonment. According to the Notice, the application was abandoned under 37 C.F.R. § 1.135 for Applicants' failure to reply to an Office action that was mailed on July 13, 2004. However, a reply was timely filed on

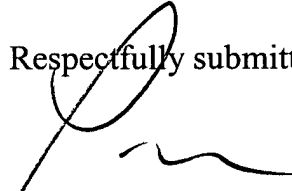
January 13, 2005. I submit that the accompanying petition to withdraw the Notice is being promptly submitted as required by 37 C.F.R. § 1.8 (b) (1).

All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date:

Feb. 2, 2005



Paul T. Clark

Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045



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Christine M. Colbert

Printed name of person mailing correspondence

Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Morey Kraus et al.	Art Unit:	1632
Serial No.:	09/698,893	Examiner:	Anne-Marie Falk, Ph.D.
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DECLARATION OF ELVIS DE LA CRUZ

I, Elvis De La Cruz, declare as follows:

I am employed by Clark & Elbing LLP. On January 13, 2005, one of my responsibilities was to ensure the delivery of firm mail to the United States Postal Service.

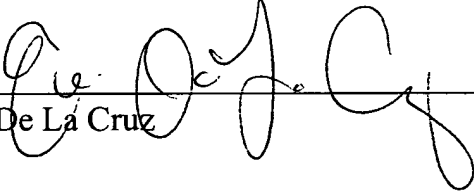
The Clark & Elbing LLP mailroom procedures that I and all other employees follow require that all mail to be taken to the Post Office be left in a specially designated box in the mailroom. The procedure in place on January 13, 2005 required that, after the close of business each day, I or another designated employee check the box for mail and

deliver it by hand to an employee of the United States Postal Service's General Mail Facility on Dorchester Avenue in Boston.

All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: 2/2/05

  
\_\_\_\_\_  
Elvis De La Cruz

Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045



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Christine M. Colbert

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Morey Kraus et al. Art Unit: 1632  
Serial No.: 09/698,893 Examiner: Anne-Marie Falk, Ph.D.  
Filed: October 27, 2000 Customer No.: 21559  
Title: METHODS FOR IMPROVING CENTRAL NERVOUS SYSTEM  
FUNCTIONING

Mail Stop Petition  
Commissioner for Patents  
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DECLARATION OF TRACEY SIMMONS  
ATTESTING TO FILING DATE UNDER 37 C.F.R. § 1.8(b)(3)  
FOR CORRESPONDENCE MAILED BUT NOT RECEIVED BY THE PTO

1. I, Tracey Simmons, am an employee of Clark & Elbing LLP.
2. I signed the certificate of mailing on the Reply to Examiner's Action and Petition for Extension of Time mailed on January 13, 2005, copies of which are enclosed.
3. I hereby attest that I had reasonable basis to believe the correspondence would be mailed on that date.
4. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title



18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: February 2, 2005

Tracey Simmons  
Tracey Simmons

Clark & Elbing LLP  
101 Federal Street  
Boston, MA 02110  
Telephone: 617-428-0200  
Facsimile: 617-428-7045



UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/698,893	10/27/2000	Morey Kraus	07588-008001	5973

7590 01/25/2005

Paul T. Clark  
Clark & Elbing, LLP  
101 Federal Street  
Boston, MA 02110

EXAMINER

FALK, ANNE MARIE

ART UNIT PAPER NUMBER

1632

DATE MAILED: 01/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

ACTION DUE PET. TO Revive  
DUE DATE 1-25-06  
INITIALS JRM

ACTION DUE Pet. to with Abandonment  
DUE DATE 3-25-05  
INITIALS JRM

RECEIVED

JAN 28 2005

CLARK & ELBING LLP



# **Notice of Abandonment**

Application No.

09/698,893

Examiner

Anne-Marie Falk, Ph.D.

Applicant(s)

KRAUS ET AL.

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

This application is abandoned in view of:

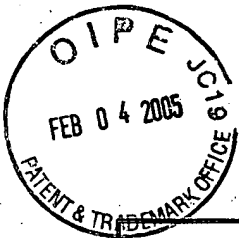
1. ☒ Applicant's failure to timely file a proper reply to the Office letter mailed on 13 July 2004.
  - (a) ☐ A reply was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply (including a total extension of time of \_\_\_\_\_ month(s)) which expired on \_\_\_\_\_.
  - (b) ☐ A proposed reply was received on \_\_\_\_\_, but it does not constitute a proper reply under 37 CFR 1.113 (a) to the final rejection.  
(A proper reply under 37 CFR 1.113 to a final rejection consists only of: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114).
  - (c) ☐ A reply was received on \_\_\_\_\_ but it does not constitute a proper reply, or a bona fide attempt at a proper reply, to the non-final rejection. See 37 CFR 1.85(a) and 1.111. (See explanation in box 7 below).
  - (d) ☒ No reply has been received.
2. ☐ Applicant's failure to timely pay the required issue fee and publication fee, if applicable, within the statutory period of three months from the mailing date of the Notice of Allowance (PTOL-85).
  - (a) ☐ The issue fee and publication fee, if applicable, was received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the statutory period for payment of the issue fee (and publication fee) set in the Notice of Allowance (PTOL-85).
  - (b) ☐ The submitted fee of \$\_\_\_\_\_ is insufficient. A balance of \$\_\_\_\_\_ is due.  
The issue fee required by 37 CFR 1.18 is \$\_\_\_\_\_. The publication fee, if required by 37 CFR 1.18(d), is \$\_\_\_\_\_.
  - (c) ☐ The issue fee and publication fee, if applicable, has not been received.
3. ☐ Applicant's failure to timely file corrected drawings as required by, and within the three-month period set in, the Notice of Allowability (PTO-37).
  - (a) ☐ Proposed corrected drawings were received on \_\_\_\_\_ (with a Certificate of Mailing or Transmission dated \_\_\_\_\_), which is after the expiration of the period for reply.
  - (b) ☐ No corrected drawings have been received.
4. ☐ The letter of express abandonment which is signed by the attorney or agent of record, the assignee of the entire interest, or all of the applicants.
5. ☐ The letter of express abandonment which is signed by an attorney or agent (acting in a representative capacity under 37 CFR 1.34(a)) upon the filing of a continuing application.
6. ☐ The decision by the Board of Patent Appeals and Interference rendered on \_\_\_\_\_ and because the period for seeking court review of the decision has expired and there are no allowed claims.
7. ☒ The reason(s) below:

On 1/18/05 the Examiner left a message for Paul Clark inquiring into whether or not a response was filed in this case but no return call was received.

*Anne-Marie Falk*

Anne-Marie Falk, Ph.D.  
Primary Examiner  
Art Unit: 1632

Petitions to revive under 37 CFR 1.137(a) or (b), or requests to withdraw the holding of abandonment under 37 CFR 1.181, should be promptly filed to minimize any negative effects on patent term.



PATENT  
ATTORNEY DOCKET NO. 07588/008001

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Tracey Simmons

Printed name of person mailing correspondence

Tracey Simmons

Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Morey Kraus et al.	Art Unit:	1632
Serial No.:	09/698,893	Examiner:	Anne Marie Falk
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Alexandria, VA 22313-1450

REPLY TO OFFICE ACTION

In reply to the non-final Office action that was mailed in connection with the above-captioned patent application on July 13, 2004, Applicants submit the following amendment and remarks.

## AMENDMENT TO THE SPECIFICATION

Please amend the specification on page 4, lines 29, through page 5, line 11, to read as follows:

Fig. 1 is a diagram illustrating a method of treating a CNS-compromised patient according to one aspect of the invention.

Figs. 2 and 3 ~~2-2A~~ illustrate methods of obtaining cells suitable for use in the invention by selection. Fig. 2 is a highly enlarged diagrammatic view illustrating a method of positive selection of a target cell. Fig. 3 ~~2A~~ is a highly enlarged diagrammatic view illustrating a method of negative selection of a non-target cell.

Fig. 4A ~~3~~ is a schematic perspective view showing a rat that has been prepared for a stroke model. Fig. 4B ~~3A~~ is a schematic diagram of an occlusion of the proximal MCA of the rat.

Fig. 5 ~~4~~ is a schematic diagram showing a rat receiving an intraparenchymal administration of stem cells.

Figs. 6-10 ~~Fig. 5~~ are graphs showing the results of behavioral tests performed on stroke model rats.

Please amend the specification on page 6, line 26, through page 7, line 3, to read as follows:

Figs. 2 and 3 2A illustrate suitable selection procedures. According to these procedures, cells of a desired target population may be substantially continuously proliferated by providing a system containing a nutrient medium in which cell proliferation can occur, and selecting cells of the target population from non-target cells in the system, concurrently with proliferation, intermittently during proliferation or following proliferation. Cell proliferation and cell selection can be carried out using an almost infinite variety of different techniques and settings, of which only a few are described below by way of example. Many other techniques will be readily perceived by those skilled in the art.

Please amend the specification on page 7, lines 20-27, to read as follows:

An example of a negative selection technique is illustrated diagrammatically in Fig. 3 2a. Briefly, one or more anti-dextran conjugated antibodies specific for a predetermined population which is not of the predetermined target population is introduced into the culture. After a specified incubation time the cell suspension is passed through a column containing dextran coated glass beads. An Antigen/Antibody/Anti-dextran/Dextran/Bead Complex forms, removing cells not of the predetermined target population from the nutrient medium. The predetermined target population is collected downstream and returned to the nutrient medium.

Please amend the specification on page 10, lines 12-24, to read as follows:

20 male Sprague Dawley rats, each weighing 300-350 grams, were anesthetized with a 2% halothane with nitrous oxide/oxygen mixture (2:1), and subjected to a MCA occlusion, using a Modified Tamura model (see Figs. 4A and 4B ~~3 and 3A~~). This stroke model has been described in the literature (see, e.g., Kawamata, T., et al., *Intracisternal Basic Fibroblast Growth Factor (bFGF) Enhances Functional Recovery and Upregulates the Expression of a Molecular Marker of Neuronal Sprouting Following Focal Cerebral Infarction*. Proc. Natl. Acad. Sci., 1997. **94**: p. 8179-8184).

The rats received cefazolin sodium i.p. (40 mg/kg) one day before surgery and immediately following surgery. 24 hours after the occlusion, all of the rats received an injection directly into the brain tissue surrounding the stroke (Figs. 5 4). 10 of the rats were injected with 1,000,000 stem cells each; the other 10 rats were injected with physiological buffered saline (PBS) vehicle. After injection, the rats were given cyclosporin i.p. each day (10 mg/kg.).

Please amend the specification on page 12, lines 19-22, to read as follows:

The results of these behavioral tests are shown in Figs. 6-10 ~~5-5D~~. The asterisks in Figs. 6 and 7 ~~5A and 5B~~ indicate that data in the stem cell groups were different from the vehicle groups by  $p < 0.05$  by two-way ANOVA (treatment X time). The lack of asterisks in Figs. 8-10 ~~5B, 5C, and 5D~~ indicate that there were no significant differences.

## AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application:

### Listing of Claims:

1. (Currently Amended) A method of causing an improvement in function of the central nervous system of a subject having impaired central nervous system function resulting from a stroke, comprising
  - (a) preparing a sample of human ~~an aliquot of~~ CD34+/-, Lin- cells derived from umbilical cord blood, wherein said CD34+/-, Lin- cells in said sample are enriched relative to CD34+/-, Lin- cells present in a mononuclear cell fraction of umbilical cord blood; and
  - (b) administering to the subject the sample ~~aliquot~~ of cells, in an amount sufficient to cause said improvement, wherein said sample ~~aliquot~~ of cells is administered directly to the site of said stroke.
  
2. (Currently Amended) A method of causing an improvement in a function of the central nervous system of a subject having impaired central nervous system function resulting from a stroke, comprising
  - (a) preparing a sample of human ~~an aliquot of~~ CD34+/-, Lin- cells derived from blood, wherein said CD34+/-, Lin- cells in said sample are enriched relative to CD34+/-, Lin- cells present in a mononuclear cell fraction of blood; and
  - (b) administering to the subject the sample ~~aliquot~~ of cells, in an amount sufficient to cause said improvement, wherein said sample ~~aliquot~~ of cells is administered



directly to the site of said stroke.

3. (Currently Amended) The method of claim 1 or 2, wherein said administering further comprises administering a growth factor to said subject.

4. (Cancelled)

5. (Currently Amended) The method of claim ~~2 or 3~~ wherein the cells are derived from peripheral blood.

6. (Currently Amended) The method of claim ~~1, 2 or 3~~ further comprising obtaining the sample aliquot of cells by separating the CD34+/-, Lin- cells ~~a desired cell population~~ from the cord blood.

7. (Original) The method of claim 3 wherein the growth factor is selected from the group consisting of oncostatin M and growth factors from the following families: FGF, neurotrophin, IGF, CNTF, EGF, TGF-beta, LIF, interleukins, PDGF and VEGF.

8. (Currently Amended) The method of claim 1 or 2 ~~1, 2 or 3~~ further comprising obtaining a sample of cells and purifying the sample to obtain the aliquot.

9. (Currently Amended) The method of claim 1 or 2 ~~1, 2 or 3~~ further comprising

~~obtaining a sample of cells and expanding at least a selected population of cells in the sample the~~  
CD34+/-, Lin- cells ~~ex vivo to obtain the aliquot.~~

10. (Currently Amended) The method of claim 1 or 2 ~~1, 2 or 3~~ wherein said sample  
~~aliquot~~ of cells comprises allogeneic cells.

11. (Currently Amended) The method of claim 1 or 2 ~~1, 2 or 3~~ wherein said sample  
~~aliquot~~ of cells comprises autologous cells.

12. (Withdrawn) The method of claim 1, 2, or 3 wherein the improvement results in  
recovery from a central nervous system trauma.

13. (Currently Amended) The method of claim 1 or 2 ~~1, 2 or 3~~ wherein the improvement  
results in repair of central nervous system damage caused by said stroke.

14. (Cancelled)

15. (Currently Amended) The method of claim 1 or 2 ~~1, 2 or 3~~ wherein the improvement  
results in regeneration of central nervous system tissue damaged by said stroke.

16-18 (Cancelled)

19. (Currently Amended) The method of claim 1 or 2 ~~1, 2 or 3~~ wherein the improvement results from a genetic element contained in the administered cells.

20. (Original) The method of claim 19 wherein the genetic element is endogenous to the administered cells.

21. (Original) The method of claim 19 wherein the genetic element has been exogenously added to the administered cells.

22. (Withdrawn) The method of claim 1, 2 or 3 wherein the improvement comprises head trauma recovery.

23. (Withdrawn) The method of claim 1, 2 or 3 wherein the improvement comprises head trauma repair.

24. (Withdrawn) The method of claim 1, 2 or 3 wherein the improvement results from tissue regeneration after head trauma.

25. (Currently Amended) The method of claim 1 or 2 wherein the cells are administered intracerebrally ~~intercerebrally~~, intracisternally, intracerebroventricularly, or intraparenchymally.

26. (Cancelled)

27. (Currently Amended) The method of claim 1 or 2 wherein the cells are characterized as: CD2<sup>-</sup>, CD3<sup>-</sup>, CD14<sup>-</sup>, CD16<sup>-</sup>, CD19<sup>-</sup>, CD24<sup>-</sup>, CD56<sup>-</sup>, CD66b<sup>-</sup>, glycophorin A<sup>-</sup>, flk-1<sup>+</sup>, CD45<sup>+</sup>, CXCR4<sup>+</sup>, or MDR<sup>+</sup>.

28. (Cancelled)

29. (Currently Amended) The method of claim 1 or 2 ~~1, 2 or 3~~ further comprising administering to the subject a cell differentiation factor.

30. (Currently Amended) The method of claim 1 or 2 ~~1, 2 or 3~~ further comprising administering to the subject a neural guidance molecule.

31. (Currently Amended) The method of claim 3 wherein the growth factor is administered intracerebrally ~~intercerebrally~~, intracisternally, intracerebroventricularly, or intraparenchymally.

32. (Currently Amended) The method of claim 3 wherein the growth factor is administered with the sample ~~aliquot~~ of cells.

33. (Currently Amended) The method of claim 3 wherein the growth factor is administered separately from the sample ~~aliquot~~ of cells.

34. (Cancelled)

35. (Previously Presented) The method of claim 13 wherein the damage caused by said stroke is due to lack of oxygen to the brain.

36. (Cancelled)

37. (Currently Amended) A method of causing an improvement in central nervous system function of a patient having impaired central nervous system function resulting from a stroke comprising:

preparing a sample of human CD34+/-, Lin- cells, wherein said CD34+/-, Lin- cells in said sample are enriched relative to CD34+/-, Lin- cells present in a mononuclear cell fraction of umbilical cord blood, obtaining an aliquot containing a predetermined target population of cells  
by

- (a) introducing a starting sample of cord blood cells into a growth medium;
- (b) causing said cord blood cells to divide;
- (c) concurrently with, intermittently during, or following step (b),

contacting the cord blood cells in the growth medium with a selection element comprising a ~~plurality~~ plurability of selective binding molecules with affinity for human CD34+/-, Lin- cord blood cells or non-CD34+/-, Lin- human ~~a first population of non-target cells~~ so as to separate human CD34+/-, Lin- cells ~~select cells of the target population~~ from other cells in the growth

medium; and

(d) administering the sample aliquot containing human CD34+/-, Lin- to the patient in an amount sufficient to cause said improvement.

38-40 (Cancelled)

41. (Original) The method of claim 37 wherein said expansion is clonogenic.

42. (Withdrawn) A method of causing an improvement in function of the central nervous system of a subject having impaired central nervous system function, comprising administering to the subject an aliquot of cells derived from umbilical cord blood, wherein the improvement results from treatment of a disease selected from the group consisting of Parkinson's Disease, Alzheimer's disease, Huntington's Disease, MS, Tay-Sachs, and cerebral palsy.

43. (Withdrawn) A method of causing an improvement in function of the central nervous system of a subject having impaired central nervous system function, comprising administering to the subject an aliquot of cells derived from blood, the aliquot containing stem cells, wherein the improvement results from treatment of a disease selected from the group consisting of Parkinson's Disease, Alzheimer's disease, Huntington's Disease, MS, Tay-Sachs, and cerebral palsy.

44. (Currently Amended) A method of causing an improvement in function of the central nervous system of a subject having impaired central nervous system function resulting from a stroke, said method comprising

(a) preparing a sample ~~an aliquot~~ of cells containing a predetermined target population by providing a starting sample of cells derived from umbilical cord blood, and causing cells of the target population in the starting sample to divide; and

(b) administering to the subject the sample ~~aliquot~~ of cells, in an amount sufficient to cause said improvement, wherein said cells are administered directly to the site of said stroke and comprise human CD34+/-, Lin- cells, and wherein said CD34+/-, Lin- cells in said sample are enriched relative to CD34+/-, Lin- cells present in a mononuclear cell fraction of umbilical cord blood.

45-47 (Cancelled)

### REMARKS

Claims 1-16, 19-25, 27, 29-33, 35, 37, and 41-44 are currently pending in this application. Claims 12, 22-24, 42, and 43 remain withdrawn from further consideration as being drawn to a non-elected invention. Claims 4, 13, and 16 are objected to for matters of form, and claims 37 and 41 are objected to as being drawn to a non-elected invention. Claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 are rejected under 35 U.S.C. § 112, first paragraph, for lack of written description and lack of enablement. Claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 are rejected under 35 U.S.C. § 112, second paragraph, for lack of clarity. Claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 are rejected under 35 U.S.C. § 102(e) for anticipation by Sanberg et al. (U.S. Patent Application Publication No. 2002/0028510 A1; hereinafter "Sanberg") in view of Rosu-Myles et al. (Stem Cells 18:374-381, 2000; hereinafter "Rosu-Myles"). Finally, the drawings are objected to due to improper labelling of the figures. By this reply, Applicants cancel claims 4, 14, and 16, amend claims 1, 2, 3, 5, 6, 8-11, 13, 15, 19, 25, 27, 29-33, 37, and 44, and address each of the Examiner's objections and rejections.

#### Support for the Amendment

Support for the amendment to claims 1, 2, 3, 5, 6, 8-11, 13, 15, 19, 25, 27, 29-33, 37, and 44 is found in the claims as originally filed and in the specification on, e.g., page 3, lines 19-26, page 5, lines 13-22, and page 6, lines 1-3. Applicants note that support for the phrase "wherein said CD34+/-, Lin- cells in said sample are enriched relative to CD34+/-, Lin- cells present in a mononuclear cell fraction of umbilical cord blood" recited in present claims 1, 2, 37, and 44 is found in the specification at page 5, lines 16-18, and in addition in Example 5 of U.S. Patent No.



5,925,567, which is incorporated by reference into the present specification. No new matter is added by the amendment.

#### Objection to the Drawings

The Examiner objects to the drawings, stating that the labeling is improper. In response, Applicants provide amended drawing sheets 1-10, corresponding to Figs. 1, 2, 3, 4A/4B, 5, 6, 7, 8, 9, and 10, respectively. The amended drawing sheets correct the improper labeling identified by the Examiner. Applicants have also made appropriate correction throughout the specification with regard to the amended figures. Therefore, Applicants request that this objection be withdrawn.

#### Claim Objections

Claims 37 and 41 are objected to for encompassing non-elected subject matter. The Examiner states that "[t]he claims are directed to treating any disorder of the central nervous system, but the elected invention is limited to methods of treating stroke" (Office Action, p. 3). Applicants have amended independent claim 37 to recite that the method of causing an improvement in central nervous system function is applied to a patient "having impaired central nervous system function resulting from a stroke." This objection may now be withdrawn.

The Examiner also objects to claims 13 and 16 under 37 C.F.R. § 1.75(c) for having improper form because the claims fail to further limit the subject matter of a previous claim. Applicants have cancelled claim 16, but respectfully disagree that claim 13 does not further limit claims 1, 2, and 3 from which it depends.

Claim 13, which has been amended to depend from claim 1 or 2, recites that the “improvement results in repair of central nervous system damage caused by said stroke.” Claim 13 further limits the subject matter of claims 1 and 2 by specifying that the “improvement” in central nervous system functioning indicated in claims 1 and 2 occurs by repairing the damage done to brain tissues as a result of the stroke. In this embodiment, the method results in the re-establishment of communication between, e.g., two or more neurons (e.g., by regrowth of axons), rather than the generation of new neurons. This is contrasted with the mode of improvement recited in claim 15, which is directed to an improvement that results due to the regeneration of brain tissues at the site of the stroke (i.e., new tissue growth). Thus, claims 13 and 15 are directed to two distinct mechanisms by which the improvement is effected, and the limitations disclosed therein serve to further limit the subject matter of claims 1 and 2. Therefore, this objection should be withdrawn.

#### Statutory Double Patenting

The Examiner indicates that should claim 1 be found allowable, claim 4 will be objected to under 37 C.F.R. § 1.75 as being a substantial duplicate thereof. Applicants have cancelled claim 4. Therefore, this objection is moot and should be withdrawn.

#### Rejections under 35 U.S.C. § 112, first paragraph

##### *Written Description*

Claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 are rejected under 35 U.S.C. § 112, first paragraph, for failing to satisfy the written description requirement. The Examiner

asserts that the specification does not disclose how to obtain "CD34+/-, Lin- cells." The Examiner further asserts that a teaching of how to obtain CD34+/-, Lin- cells that is based on a method incorporated by reference from U.S. Patent No. 5,925,567 is not sufficient to satisfy the written description requirement because the '567 patent only discloses how to obtain CD34- cells. Thus, the Examiner concludes:

Given that the specification discloses that the cell composition used in the Example comprises "CD34+/-, Lin- cells," one of skill in the art would not know the identify of the cell composition that produced the result described therein... Thus it is concluded that the written description requirement is not satisfied for the claimed methods of cell transplantation. (Office Action, p. 6.)

Applicants respectfully traverse this rejection.

Contrary to the Examiner's conclusion, the term "CD34+/-, Lin-" clearly and unambiguously identifies the target population of cells recited in claims 1, 2, 37, and 44, and claims dependent therefrom. Applicants have chosen this shorthand designation, which is used and understood by those skilled in the art, to specify the cell surface markers that are present (+) or absent (-) on the recited population of cells, and which distinguish those cells from other cells. The cells recited in claims 1, 2, and 44, and claims dependent therefrom, are characterized by the presence or absence of CD34 (CD34+/-; i.e., both populations of cells are present) and the absence of lineage-specific markers (Lin-; i.e., the cells are undifferentiated). An alternative designation, using less abbreviated shorthand, would be to identify the target population of cells as including CD34+, Lin- cells and CD34-, Lin- cells. However, if the Examiner believes it would expedite prosecution, Applicants' are willing simply to delete "CD34+/-" from the claims.

This shorthand method of characterizing target cells by using (+) and (-) designations

was, at the time of invention, conventional in the art. For example, Gallacher et al. (Blood, 95:2813-2820, 2000; a copy of which is provided) employed this designation. Gallacher et al. refers to both CD34<sup>+</sup>, Lin<sup>-</sup> cells and CD34<sup>-</sup>, Lin<sup>-</sup> cells (Gallacher et al. also defines the cells using the CD38<sup>-</sup> designation), stating:

Novel subpopulations identified within both CD34-CD38-Lin<sup>-</sup> and CD34<sup>+</sup>CD38-Lin<sup>-</sup> fractions were isolated based on the absence or presence of detectable cell surface CD7 or AC133 expression using sorting gates as indicated in Figure 1. (See p. 2815, col. 2.)

In addition, the specification further defines the "CD34<sup>±</sup>, Lin<sup>-</sup> cells" of interest by stating that they are "characterized as: CD2<sup>-</sup>, CD3<sup>-</sup>, CD14<sup>-</sup>, CD16<sup>-</sup>, CD19<sup>-</sup>, CD24<sup>-</sup>, CD56<sup>-</sup>, CD66b<sup>-</sup>, glycophorin A<sup>-</sup>, Flk-1<sup>+</sup>, CD45<sup>+</sup>, CXCR4<sup>+</sup>, MDR<sup>+</sup>" (see, e.g., page 6, lines 18-20).

Applicants' specification employs completely conventional nomenclature for characterizing the target cell population; the skilled artisan would have no uncertainty with respect to the identity of the cell composition used in the method of the present claims. Therefore, the terminology used to describe the recited cell composition is not unclear and need not be defined in Applicants' specification in any more detail than is provided.

The Examiner also asserts that the specification does not describe the preparation of CD34<sup>±</sup>, Lin<sup>-</sup> cells for use in the method of claims 1, 2, 37, and 44, and claims dependent therefrom, pointing to the absence in Example 5 of U.S. Patent No. 5,925,567, which is incorporated by reference into Applicants' specification, of a specific description of the preparation of CD34<sup>±</sup>, Lin<sup>-</sup> cells. Applicants clarify that Example 5 of the '567 patent discloses a negative selection method that can be used to separate cells expressing CD2, CD3, CD14, CD16, CD19, CD24, CD56, CD66b and glycophorin A from cells that do not express

these markers, so that the cells lacking the specified markers can be collected (see col. 16, lines 43-51). Although the '567 patent does not specify that the cells lacking expression of CD2, CD3, CD14, CD16, CD19, CD24, CD56, CD66b and glycophorin A are lineage-negative (Lin-) cells, this feature is disclosed in the present specification, which defines CD34+/-, Lin- cells as being cells that do not express CD2, CD3, CD14, CD16, CD19, CD24, CD56, CD66b, and glycophorin A (see, e.g., page 6, lines 18-20). Because an anti-CD34 antibody is not used in the selection method of the '567 patent, the cells that are collected include both CD34+ and CD34- cells. Therefore, the method disclosed in Example 5 of the '567 patent would result in the preparation of a cell population within claims 1, 2, 37, and 44 of the present application, and claims dependent therefrom. Thus, Applicants' specification adequately conveys to one skilled in the art that Applicants, as of the filing date of the application, were in possession of the cell compositions required for use in the methods of claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44. For all of the reasons provided above, Applicants submit that the written description requirement has been met, and respectfully request that the rejection of claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 under 35 U.S.C. § 112, first paragraph, be withdrawn.

#### *Enablement*

Claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 are also rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner states that "the specification does not teach how to use the claimed methods to produce a therapeutic effect nor does it adequately teach how to practice the claimed method, which covers transplantation of a variety of cell types, as well as combined administration of cells and growth factors" (Office Action, p. 8).

Specifically, the Examiner states that the specification fails to provide guidance regarding the cell compositions to be used in transplantation (i.e., the type of cells and the species from which the cells are obtained), and how to obtain a beneficial effect following transplantation (Office Action, p. 7). The Examiner concludes by stating that "methods of transplantation of stem cells, precursor cells, and neural tissue into the CNS are not routinely successful and the specification does not offer adequate guidance to overcome the unpredictability in the art to...derive a therapeutic benefit in a diseased animal" (Office Action, p. 8). Applicants respectfully disagree.

The specification provides considerable guidance with respect to the cells to be administered and how to obtain those cells. As is discussed above, the type of cells to be transplanted, designated as CD34+/-, Lin- cells using conventional nomenclature employed in the art, are clearly and unambiguously identified by Applicants' specification. Because this designation would be understood by the skilled artisan, no undue experimentation would be required of the skilled artisan to obtain the cells. Applicants have also amended independent claims 1, 2, 37, and 44 to specify that the CD34+/-, Lin- cells are human cells, a limitation which is clearly described in the specification on page 2, lines 24-27. Finally, as is also discussed above, U.S. Patent No. 5,925,567, which is incorporated by reference into the present specification, provides considerable guidance with respect to the preparation of human CD34+/-, Lin- cells for use in the methods of claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44. Therefore, these issues raised by the Examiner to support the enablement rejection of claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 are moot.

The specification also teaches one skilled in the art how to obtain a beneficial effect following transplantation of the CD34+/-, Lin- cells according to the methods of claims 1-11, 13-

16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44. Applicants direct the Examiner to page 10, line 9 through page 13, line 7, of the specification, which teaches that significant improvement in central nervous system functioning in Sprague Dawley rats subjected to middle cerebral artery (MCA) occlusion, i.e., a rat stroke model, results when the treated rats were administered 1,000,000 human CD34+/-, Lin- stem cells by injection directly to the site of the stroke. The specification teaches that the MCA-occluded rats administered stem cells showed significant improvement in CNS function as compared to MCA-occluded rats administered vehicle alone, as determined using the forelimb placing test and the hindlimb placing test (see page 10, line 9, through page 13, line 7). Moreover, because the improvement in the MCA-occluded rat model is art-recognized as being predictive of success in treating stroke in humans (see, e.g., page 10, lines 14-18, of the specification), Applicants' statistically significant results of improvement in the MCA-occluded rat model plainly support the enablement of the method of present claims 1, 2, 37, and 44, and claims dependent therefrom, which recite improvement in humans.

Applicants also direct the Examiner to the Declaration of Dr. Finklestein, which was filed on April 18, 2003, as evidence that CD34+/-, Lin- cells recited in claims 1, 2, 37, and 44, when administered to an area of brain disease or damage due to stroke, bring about an improvement in CNS function. The Declaration of Dr. Finklestein confirms that the administered CD34+/-, Lin- cells are able to effectively treat stroke when administered intravenously (i.e., requiring the cells to migrate to the site of damage) and when administered directly to the brain (see paragraph 4 of the Declaration of Dr. Finklestein filed on April 18, 2003).

Finally, Applicants note that the Examiner has previously acknowledged the enablement of claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44. Applicants direct the Examiner

to page 3 of the Office Action mailed July 1, 2003, where the Examiner states that the specification is enabling for:

...a method of causing improvement in function of the central nervous system in a mammal having brain ischemia resulting from stroke, comprising injecting CD34+/-, Lin- cells into an ischemic region of the mammal's brain...

The Examiner further states:

The Declaration of Dr. Finklestein has been fully considered and the Examiner accepts that the example therein demonstrates that intravenous administration of umbilical cord blood cells in combination with a growth factor did result in functional improvement. (See page 4 of the Office Action dated July 1, 2003.)

Therefore, based on the teachings in the specification, and as elaborated in the Declaration of Dr. Finklestein, a skilled artisan would appreciate that administration of human CD34+/-, Lin- stem cells directly to the site of stroke damage would result in improvement in CNS function. Because the methods taught in Applicants' specification clearly enable one skilled in the art to practice the full scope of the claimed invention without requiring undue experimentation, as is discussed above, Applicants submit that the scope of present claims 1-3, 5-11, 13, 15, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 is commensurate with the level of skill in the art and undue experimentation would not be required to practice the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 under 35 U.S.C. § 112, first paragraph, be withdrawn.



Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 are rejected under 35 U.S.C. § 112, second paragraph. The Examiner states that claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, and 44 are indefinite because “the term ‘CD34+/-, Lin-’ is not defined in the specification and is not conventional in the art. Thus, it is unclear what the ‘CD34+/-’ designation means. It is therefore unclear what cell type is to be used in the claimed method” (Office Action, p. 10).

As is discussed above, the designation “CD34+/-, Lin-” is not unclear or ambiguous. Rather, this term is conventional in the art and clearly identifies the cells for use in the method of present claims 11-3, 5-11, 13, 15, 19-21, 25, 27, 29-33, 35, 37, 41, and 44. These cells express the cell surface marker CD34 (i.e., the cells are “CD34+”) or lack expression of CD34 (i.e., they are “CD34-”) and do not express the lineage markers (i.e., the cells are “Lin-”). Thus, CD34+/- indicates either expression or lack of expression of CD34. Because this term is a clearly understood and technically recognized designation, this rejection should be withdrawn.

The Examiner also rejects claim 14, stating that the “recitation of ‘central nervous system disease caused by said stroke’ ... [is indefinite] because stroke does not **cause** CNS disease. Stroke is typically a **result of** cerebrovascular disease” (Office Action, p. 10; emphasis in original). Applicants have cancelled claim 14. This rejection can now be withdrawn.

Claims 25 and 31 are rejected for lack of clarity for reciting “intercèbrally,” which is not defined in the specification and would be unclear in its use. Applicants have amended claims 25 and 31 to recite “intracerebrally” to correct this typographical error. “Intracerebral,” which is an art-known term, is defined by Merriam-Webster Online Dictionary as “situated in, introduced into, or made into the cerebrum” (Merriam-Webster Online Dictionary, 2005). Because this term

is not unclear and is art-recognized, this rejection can now be withdrawn.

The Examiner also rejects claims 25 and 31 for reciting “intercerebrally,” “intracisternally,” and “intracerebrovascularely,” stating that “[c]laims 1 and 2, from which claims 25 and 31 depend, are already limited to administering the cells ‘directly to the site of said stroke.’ The ‘site of said stroke’ would necessarily be located within the brain tissue and therefore would not be located in the fluid-filled spaces such as the ventricles” (Office Action, p. 11). Applicants respectfully disagree that the site of a stroke is limited to brain tissue and does not include, e.g., the fluid-filled ventricles, as is asserted by the Examiner.

A stroke occurs when brain cells (e.g., neurons) are deprived of oxygen-rich blood (cerebral ischemia), usually due to the presence of a blood clot in one or more arteries of the brain. A stroke can also result from bleeding into or around the brain (cerebral hemorrhage), which also deprives brain tissue of oxygen-rich blood. Therefore, the site of a stroke includes not only the brain tissue damaged due to the lack of oxygen (e.g., the region surrounding the clogged artery and the region downstream of the clogged artery in the case of cerebral ischemia), but also the region of damage (i.e., the site of hemorrhage). Accordingly, present claims 25 and 31 clarify that the administration of a cell sample containing an enriched CD34+/-, Lin- cell population alone, or in conjunction with a growth factor, respectively, to the site of the stroke includes intracerebral, intracisternal, intracerebroventricular, or intraparenchymal administration.

Any one of these methods of administration would position the administered cells and growth factor in proximity to the site of the stroke; a fact that would be understood by the skilled artisan.

Therefore, claims 25 and 31 do not lack clarity, and Applicants respectfully request that the rejection of these claims under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 are rejected under 35 U.S.C. § 102(e) for anticipation by Sanberg in light of Rosu-Myles. The Examiner states that “Sanberg et al. (2000) disclose a method for treating stroke by administering umbilical cord blood cells...[and that] [t]he disclosure explicitly contemplates using the method of the invention to treat stroke (paragraphs [0042], [0054], [0065], and paragraphs [0161] through [0233]” (Office Action, p. 12). The Examiner further states that “[t]he reference of Sanberg et al. inherently discloses the administration of a cell composition comprising Lin- cells, as recited in the claims, because human cord blood cells inherently comprise Lin- cells, as evidenced by Rosu-Myles et al.” (Office Action, p. 12).

Applicants have amended claims 1, 37, and 44 to recite the preparation of a cell sample containing an enriched population of CD34+/-, Lin- cells, relative to the amount of CD34+/-, Lin- cells present in a mononuclear cell fraction of UCB, and claim 2 to recite the preparation of a cell sample containing an enriched population of CD34+/-, Lin- cells, relative to the amount of CD34+/-, Lin- cells present in a mononuclear cell fraction of blood. Sanberg fails to teach or suggest the preparation of a cell sample containing an enriched population of CD34+/-, Lin- cells, relative to the amount of CD34+/-, Lin- cells present in a mononuclear cell fraction of UCB or blood. Sanberg also fails to teach or suggest the preparation of any cell population from a source other than umbilical cord blood (UCB), such as blood, which is recited in present claim 2, or peripheral blood, which is recited in Applicants' claim 5.

Sanberg merely describes the preparation and administration of neural cells from whole

UCB, a mononuclear cell fraction thereof, or a mononuclear cell fraction that has been treated with a mitogenic agent or a differentiation factor to increase the population of, or differentiation to, neural cells (see, e.g., pages 3-4, paragraph [0032], and page 13, paragraph [0139]). Sanberg defines "neural cells" as follows:

The term "neural cells" are cells having at least an indication of neuronal or glial phenotype, such as staining for one or more neuronal or glial markers or which will differentiate into cells exhibiting neuronal or glial markers. Examples of neuronal markers which may be used to identify neuronal cells according to the present invention include, for example, neuron-specific nuclear protein, tyrosine hydroxylase, microtubule associated protein, and calbindin, among others. The term neural cells also includes cells which are neural precursor cells, i.e., stem and/or progenitor cells which will differentiate into or become neural cells or cells which will ultimately exhibit neuronal or glial markers, such term including pluripotent stem and/or progenitor cells which ultimately differentiate into neuronal and/or glial cells. (See page 5, paragraph [0053].)

As is discussed above, the designation "Lin-" indicates that the cells for use in the method of present claims 1, 2, 37, and 44, and claims dependent therefrom, lack lineage-specific markers, such as neural cell-specific markers. Therefore, the CD34+/-, Lin- cells recited in present claims 1, 2, 37, and 44 can be distinguished from the "neural cells" of Sanberg because the CD34+/-, Lin- cells are undifferentiated and do not have "an indication of neuronal or glial phenotype." Furthermore, Sanberg fails to teach or suggest that the whole UCB preparation, the mononuclear cell fraction preparation, or the mononuclear cell fraction preparation that has been treated with a mitogenic agent or a differentiation factor contains an enriched population of CD34+/-, Lin- cells. The term "whole" indicates that the whole UCB preparation is prepared and administered without enrichment of any population of cells therein, such as by fractionation,

separation, or purification. Because the present claims recite providing a sample of cells enriched in CD34+/-, Lin- cells relative to a mononuclear cell fraction of UCB (independent claims 1, 37, and 44) or blood (independent claim 2), the disclosure by Sanberg of the administration of whole UCB does not teach or suggest the method of present claims 1-3, 5-11, 13, 15, 19-21, 25, 27, 29-33, 35, 37, 41, and 44.

With respect to the mononuclear cell fraction of UCB, Sanberg clearly states that it includes either all of the mononuclear cells (i.e., no enrichment for CD34+/-, Lin- cells), or that it lacks CD34+ cells. Sanberg states that the “[i]nitial experiments with umbilical cord blood utilize all of the mononuclear cells collected without separation of CD34+ cellular components...[while] [o]ther experiments utilize cord blood that is depleted of CD34+ cells” (see, e.g., page 10, paragraph [0091]; emphasis added). Sanberg fails to teach or suggest that the mononuclear cell fraction prepared from UCB contains an enriched population of CD34+/-, Lin- cells, and, in fact, Sanberg advocates removing the CD34+ cells; cells which are present in the cell composition recited in present claims 1, 2, 37, and 44, and claims dependent therefrom. Thus, Sanberg not only fails to teach or suggest preparing and using an enriched population of CD34+/-, Lin- cells, as is recited in the present claims, Sanberg also fails to provide any motivation to enrich CD34+/-, Lin- cells for use in treating stroke.

Sanberg further discloses that the mononuclear cell fraction can be modified by exposure to “neural proliferation medium,” which contains a mitogenic agent, such as EGF and bFGF (see, e.g., page 13, paragraph [0139]). This cell composition is enriched for “neural and mesenchymal precursors,” which are identified by the expression of neural cell-specific markers, such as nestin and vimentin, not CD34+/-, Lin- cells which lack these neural cell-specific markers (see page 7,

paragraph [0062], and pages 10-11, paragraph [0098]). Because these neural cell-specific markers are absent in CD34+/-, Lin- cells, as is evidenced by the designation "Lin-," this limitation in the present claims further serves to distinguish the cell composition of Sanberg from the cell composition recited in independent claims 1, 2, 37, and 44, and claims dependent therefrom.

Finally, Sanberg describes treating a mononuclear cell fraction with "neural differentiation medium," which contains a differentiation factor, such as retinoic acid (RA) and neural growth factor (NGF), and which promotes differentiation of the neural cells (see, e.g., page 13, paragraph [0139]). Sanberg states that "[c]ord blood cells, cultured in the presence and absence of retinoic acid (RA) and Nerve Growth Factor (NGF), gave rise to cells bearing neural progenitor markers as evidenced by profiles of gene and protein expression" (see page 14, paragraph [0152] and Table I). Again, these cells, like the neural and mesenchymal precursors cells produced upon exposure of a mononuclear cell fraction to a mitogen, are distinguished from the enriched CD34+/-, Lin- cell population recited in independent claims 1, 2, 37, and 44, and claims dependent therefrom, because the differentiated neural cells clearly express lineage-specific markers that are absent in the undifferentiated, non-neural-specific CD34+/-, Lin- cells.

As is evident from the discussion above, Sanberg alone clearly fails to expressly teach or suggest the preparation of a cell sample containing an enriched population of CD34+/-, Lin- cells. The Examiner also raises the issue of inherency, stating that Sanberg "inherently discloses administration of a cell composition comprising Lin- cells, as is recited in the claims, because human cord blood cells inherently comprise Lin- cells, as evidenced by Rosu-Myles et al. (Office Action, p. 12). Because Sanberg fails to teach or suggest the preparation of an enriched

population of CD34+/- cells, Lin- cells, the issue of inherency is moot, because neither Sanberg nor Rosu-Myles teaches or suggests this element of present claims 1, 2, 37, and 44, and claims dependent therefrom. Therefore, for all of the reasons discussed above, Sanberg, either alone or in combination with Rosu-Myles, fails to disclose each and every limitation of present claims 1-3, 5-11, 13, 15, 19-21, 25, 27, 29-33, 35, 37, 41, and 44, and the requirements for establishing anticipation have not been met (see M.P.E.P. § 2131). Accordingly, Applicants respectfully request that the rejection of claims 1-11, 13-16, 19-21, 25, 27, 29-33, 35, 37, 41, and 44 be withdrawn.

CONCLUSION

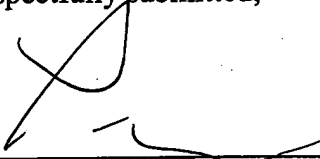
In light of the foregoing amendment and remarks, Applicants submit that the claims are in condition for allowance.

Enclosed is a Petition to extend the period for replying for three months, to and including January 13, 2005, and a check for the fee required under 35 U.S.C. § 1.17(a).

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: Jan. 13, 2005

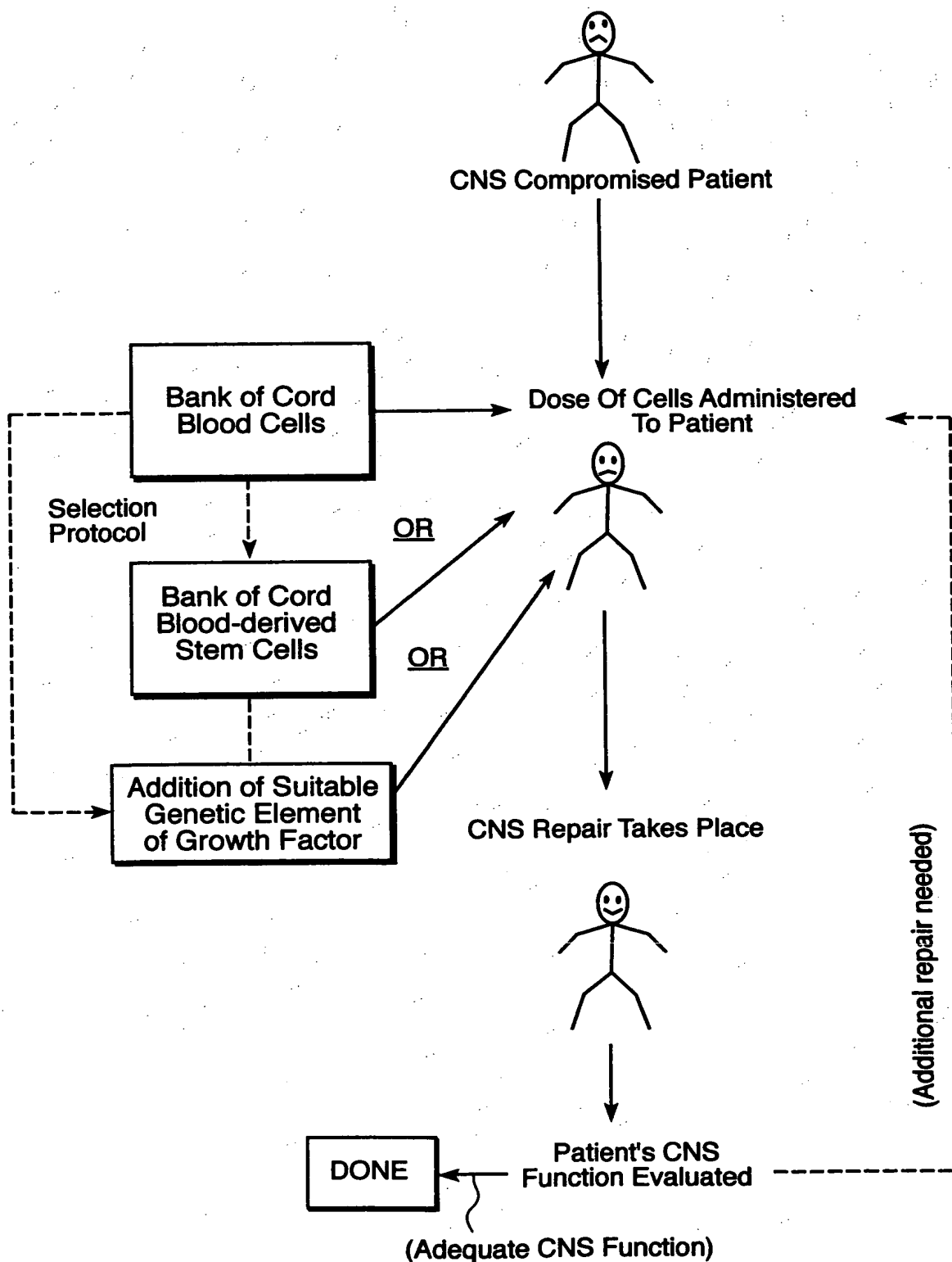
  
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FIG. 1



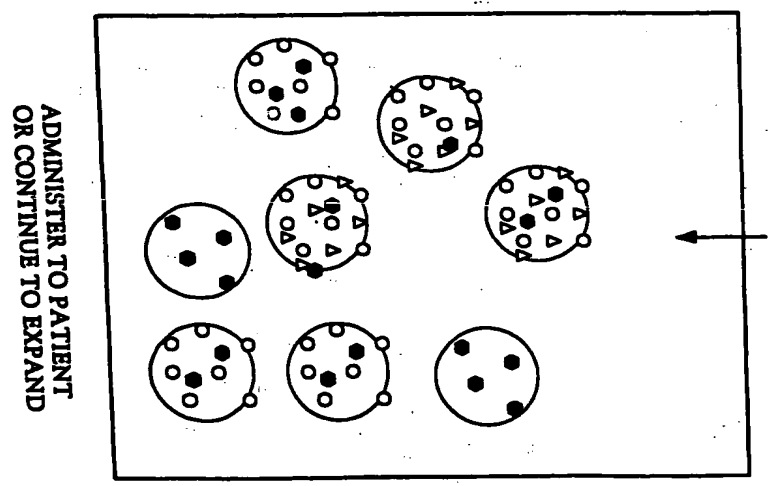
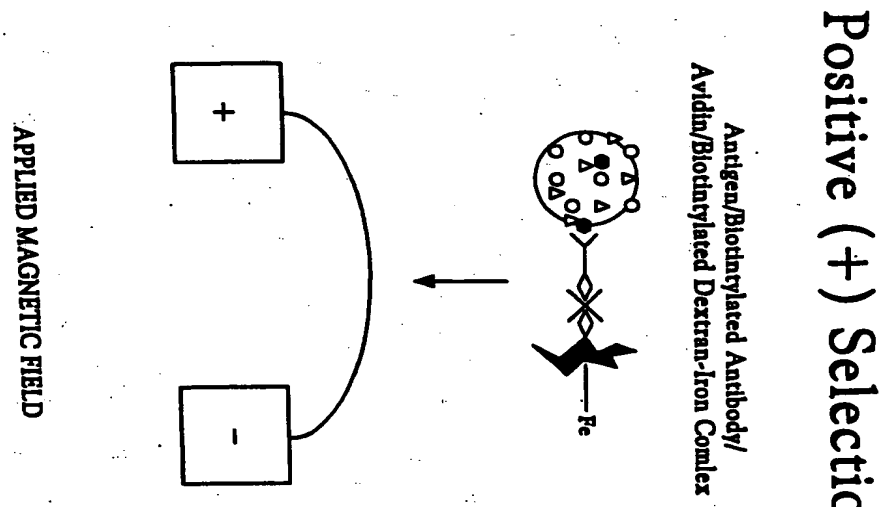
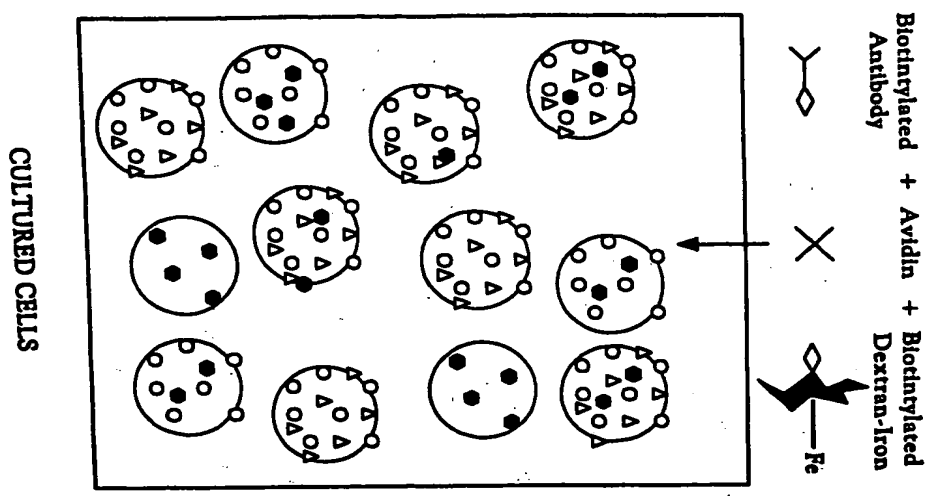


FIG. 2

● Antigen specific to predetermined target population



## Negative (-) Selection

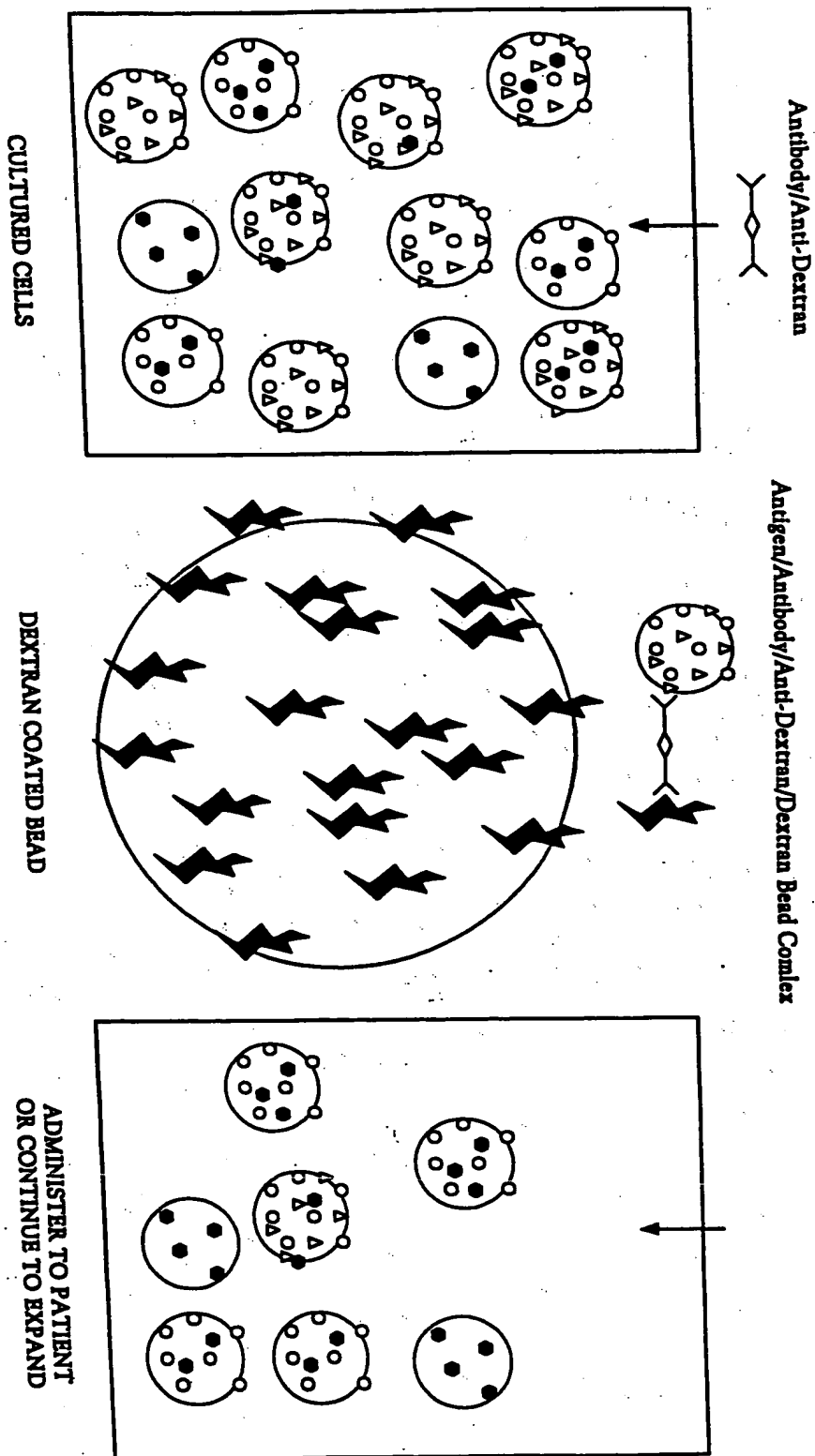




FIG. 4A

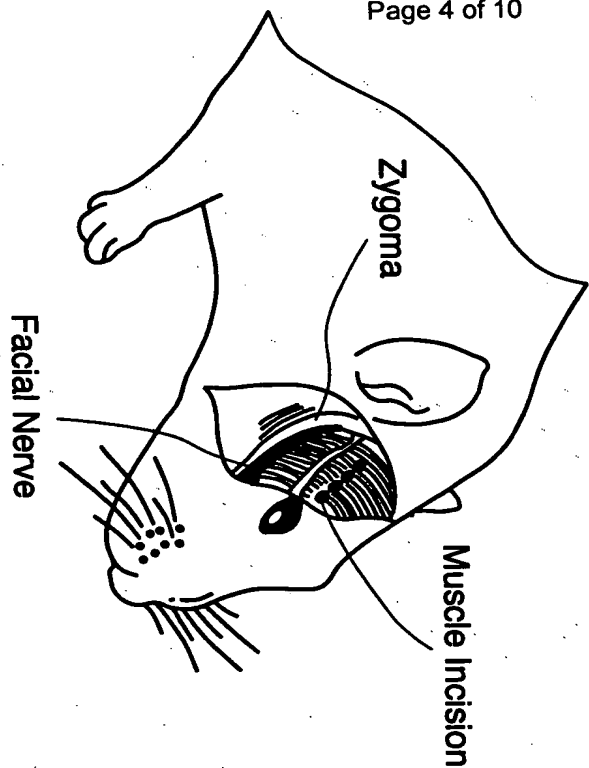
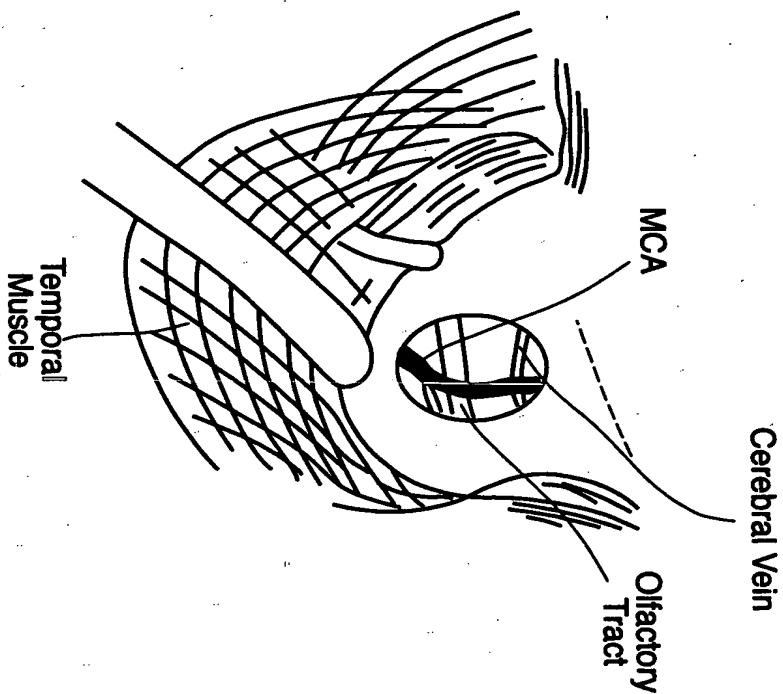


FIG. 4B



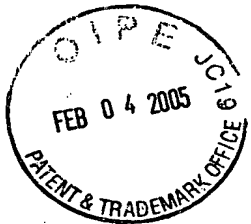


FIG. 5

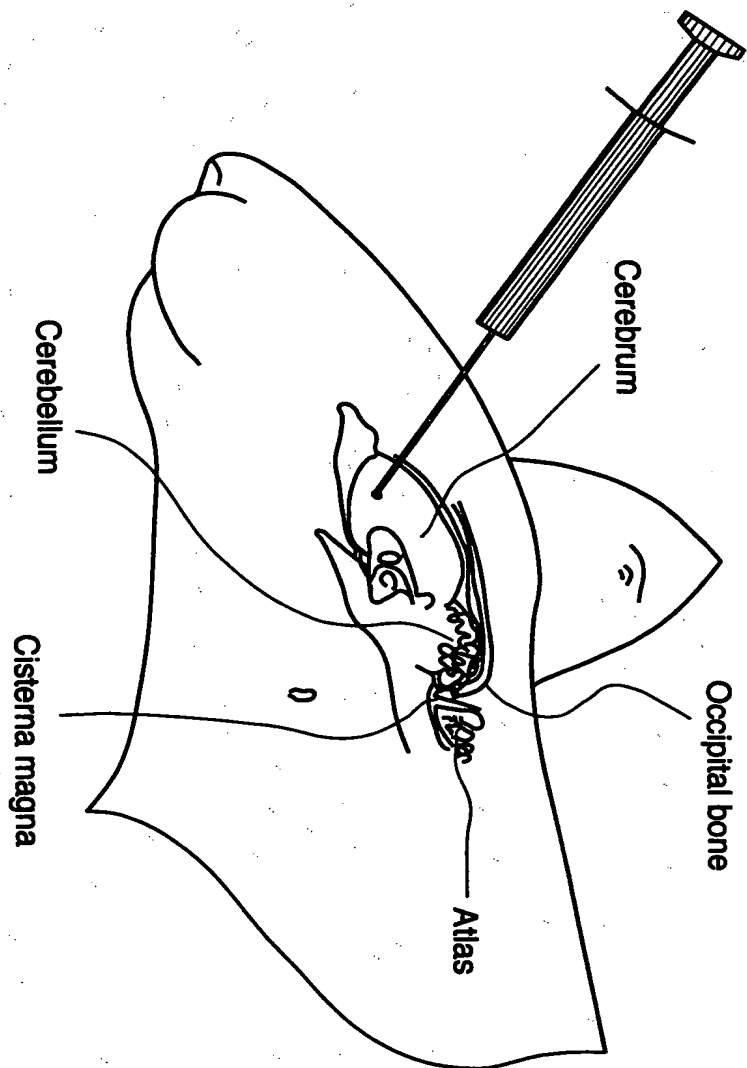
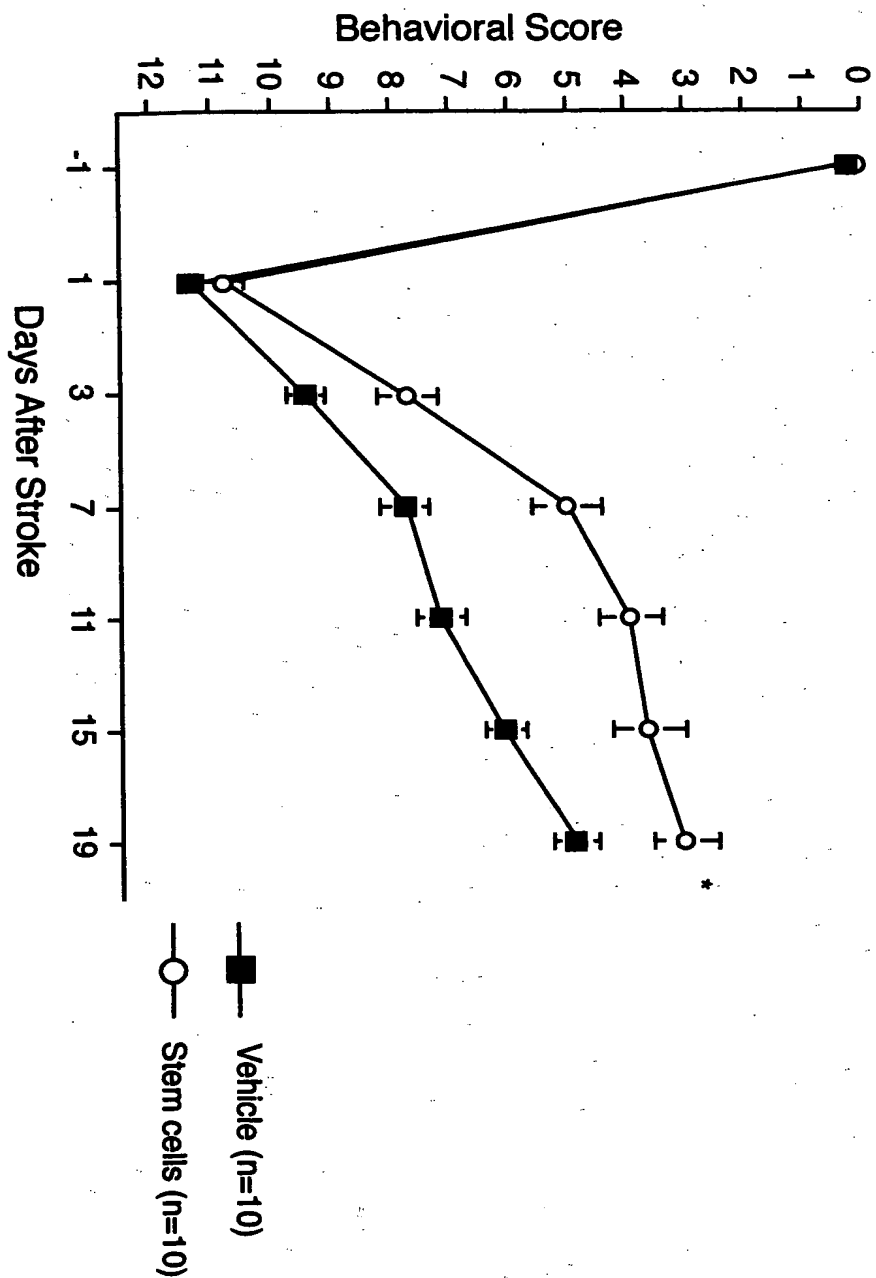




FIG. 6



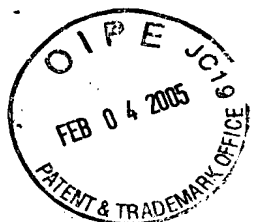


FIG. 7

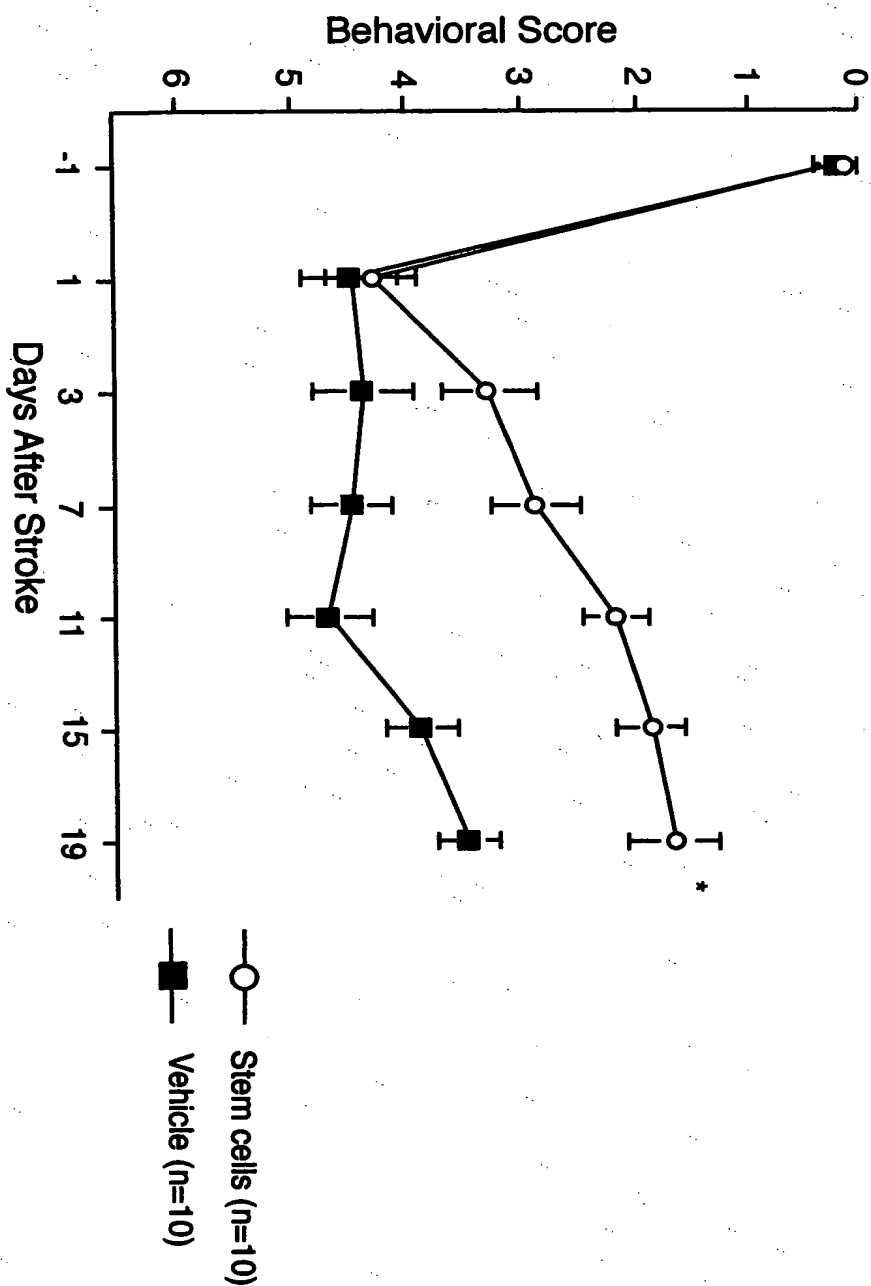
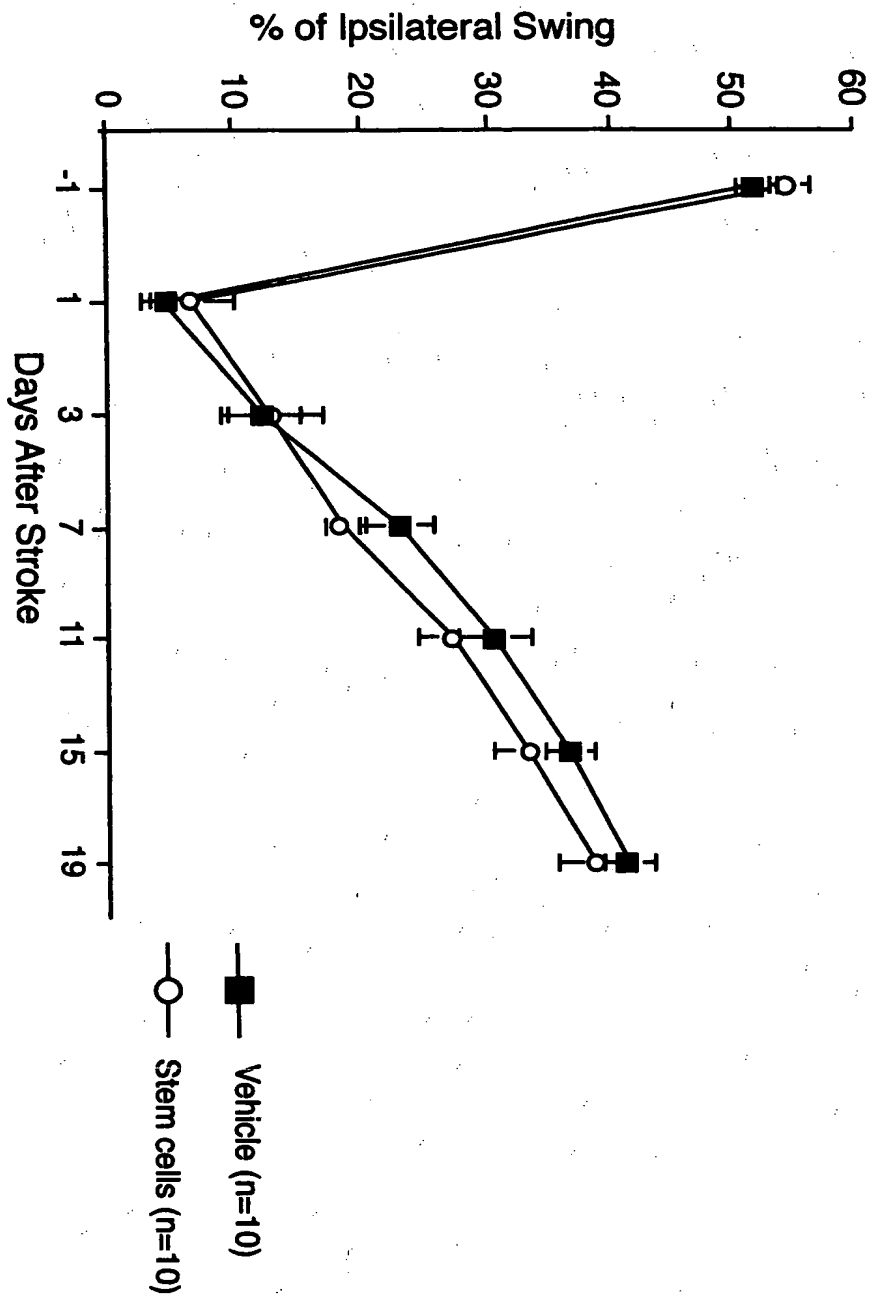




FIG. 8





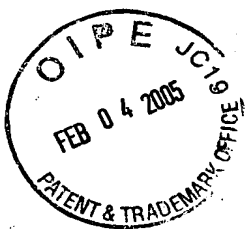
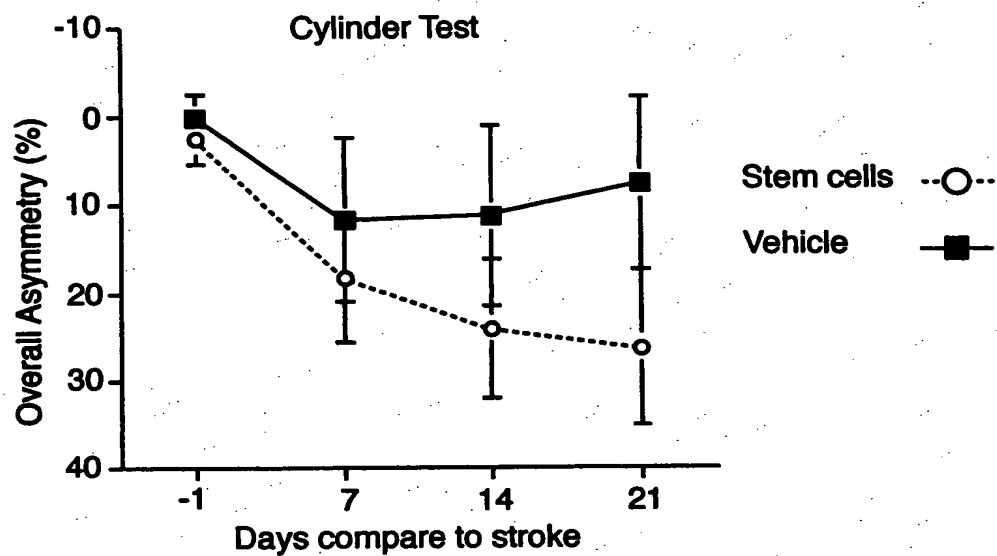
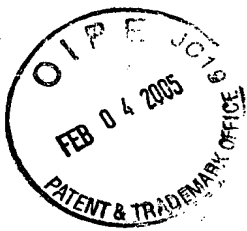
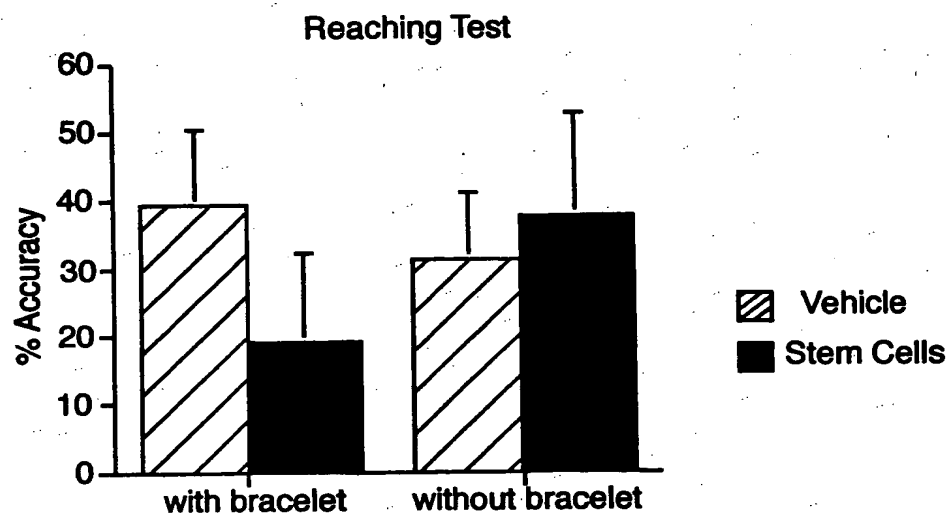


FIG. 9





**FIG. 10**





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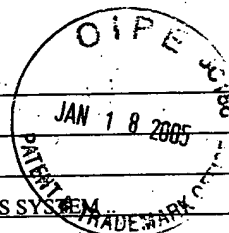
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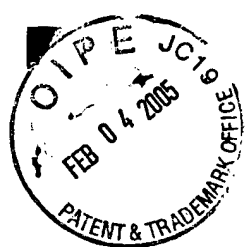


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Applicant:	Morey Kraus et al.	Art Unit:	1632
Serial No.:	09/698,893	Examiner:	Anne Marie Falk
Filed:	October 27, 2000	Customer No.:	21559
Title:	METHODS FOR IMPROVING CENTRAL NERVOUS SYSTEM FUNCTIONING		

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PETITION FOR EXTENSION OF TIME

Pursuant to 37 C.F.R. § 1.136, Applicants hereby petition that the period for replying to the Office action that was mailed in connection with the above-captioned application on July 13, 2004 be extended for three months, to and including January 13, 2005.

Enclosed is a check for \$510.00 for the fee required by 37 C.F.R. § 1.17(a).


If there are any other charges or any credits, please apply them to Deposit Account

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Respectfully submitted,

Date:

Jan. 13, 2005

  
\_\_\_\_\_  
Paul T. Clark

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